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PRESENTATION

Operator

Good morning. My name is Kevin, and I'll be the operator today. Welcome to Moderna's Fourth Quarter and Full Year 2021 Earnings Call. (Operator Instructions) Please be advised that this call is being recorded.

At this time, I'd like to turn the call over to Lavina Talukdar, Head of Investor Relations at Moderna. Please proceed.

Lavina Talukdar - *Moderna, Inc. - Senior VP & Head of IR*

Thank you, Kevin. Good morning, everyone, and thank you for joining us on today's call to discuss Moderna's fourth quarter and full year 2021 financial results and business update. You can access the press release we issued this morning as well as the slides that we'll be reviewing by going to the Investors section of our website. On today's call are Stephane Bancel, our Chief Executive Officer; David Meline, our Chief Financial Officer; Stephen Hoge, our President; and Paul Burton, our Chief Medical Officer.

Before we begin, please note that this conference call will include forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Please see Slide 2 of the accompanying presentation and our SEC filings for important risk factors that could cause our actual performance and results to differ materially from those expressed or implied in these forward-looking statements.

With that, I will turn over the call to Stephane.

Stephane Bancel - *Moderna, Inc. - CEO & Director*

Thank you, Lavina. Good morning or good afternoon, everyone. Welcome to our Q4 2021 conference call.

Today, I will start by a quick business review of fiscal year '21 before Paul walks you through some real-world evidence later. Stephen will then review our clinical programs before David presents our financial results. I will then come back to close, to share some thoughts about where we are heading.

We are pleased to report today $18.5 billion of revenues for fiscal year 2021 and a GAAP net income of $12.2 billion, translating into a GAAP diluted earnings per share of $28.29 billion, with a cash balance at the end of the year of $17.6 billion. We announced this morning that we have completed our August 2021 $1 billion share buyback plan, which reduced our average share count during the fourth quarter for the first time in the company history.

I am very proud of our team's ability to advance as well as expand with new programs our development pipeline. In respiratory vaccines, for COVID, as you know, we received full BLA approval from the U.S. FDA for Spikevax. With authorization for 12 to 17 years old in key markets globally, we are running a 50-microgram dose study in the U.S. for adolescents following discussions with the FDA. We are pleased to report that we have also started to receive authorization for children aged -- 6 to 11 years of age, beginning in Australia last week, with more countries expected in the days and weeks to come.

We also dosed our first participants in our Omicron-specific vaccine trial, mRNA-1273.529. And today, we're announcing that we plan to bring mRNA-1273.214, a bivalent vaccine combining the wild-type vaccine mRNA1273 and the Omicron vaccine mRNA1273.529 into one single dose booster, into the clinic with total mass of 50 micrograms. We are very excited that now RSV is in Phase III. This is our third vaccine starting the Phase III. And for flu, we are waiting the Phase II data for mRNA1010. As soon as we have them, we will pick a dose and will initiate our Phase III for flu and we will start our Phase I for COVID plus flu program, mRNA1273.

For latent viruses, CMV is enrolling in Phase III, EBV and HIV are now in Phase I. And we are very excited to announce last week that we are adding 2 new latent virus programs to our development pipeline, one vaccine against HSV and one vaccine against VZV. More latent viruses vaccines are in the works in our labs.

In therapeutics, PA and MMA are in the clinic, dosing and recruiting more patients. We announced a new checkpoint cancer vaccine, mRNA-4359. And Merck has informed us that they are returning the rights to the KRAS vaccine while evaluating future steps for this program.

The company continues to expand at a rapid pace. We now have one approved medicine; 2 in Phase III, RSV and CMV; and 5 in Phase II, for a total of 44 programs. We are deploying capital to accelerate and expand the pipeline. The company now has 3,000 team members across the world with a great culture and 11 commercial subsidiaries across Americas, Europe and Asia Pacific. Our $17 billion cash balance at the end of the year is enabling us to scale across research, development, manufacturing, commercial and G&A.

With this, let me now turn to Paul.

Paul Burton - *Moderna, Inc. - Chief Medical Officer*

Thank you, Stephane, and hello, everyone. It is almost exactly 3 months ago that we first heard about the [Omicron variant]. And today, we look back on 3 months that have seen millions of new cases of COVID-19 infection worldwide due to Omicron and a death toll that turned out to be almost 20% higher than that seen during the Delta wave. It is clear that SARS-CoV-2 is a virus capable of making very large evolutionary leaps in its structure and function. And while we are hopeful that we are about to enter a period of relative stability in the Northern Hemisphere, we believe firmly that a vaccine booster dose will be required for the fall of 2022 to provide ongoing protection against this virus.

We have seen measures taken by the United Kingdom recently to offer an additional booster dose to those at higher risk. And we believe such measures will become more widespread with governments looking to protect their populations from disease later this year and support their health care systems. As always, a huge note of appreciation to the frontline workers, the health care workers who have continued to immunize us and protect us during this pandemic. Their tireless work has saved millions of lives worldwide.

I'm going to review some data today that underpins why we believe an additional booster shot will be required certainly by the fall of 2022. First, let me share with you some data from a study of almost 440,000 individuals in the United States Veterans Administration database looking at the effectiveness of mRNA-1273, Spikevax, used in the primary series vaccination setting. As we know, the mRNA vaccines are extremely safe and effective, and the data here show the exceptional effectiveness of mRNA-1273.

In this well-powered and prospectively designed comparative effectiveness study, mRNA-1273 significantly reduced the risk of COVID-19 infection and hospitalization compared to BNT162b2. These data are reassuring and continue to underpin the strong global confidence that governments, health care systems and individuals have in mRNA COVID-19 vaccines and mRNA-1273. Indeed, an example of that is the very recent announcement by the CDC at British Columbia for the preferential use of the Moderna vaccine in anyone over 12 years of age living with the immunocompromised.

A similar pattern of results are seen from real-world effectiveness studies in the United Kingdom. The graphs I'm going to show you here come from the United Kingdom Health Security Agency, looking at the effect of either the Pfizer-BioNTech or Moderna vaccines and their vaccine effectiveness against hospitalization. First, let me show you the results in people who for their primary vaccination received the Pfizer-BioNTech vaccine and were then boosted with either the Pfizer-BioNTech vaccine or the Moderna vaccine. We see retained protection against the Delta variant of concern in the field squares but we see waning of effect in the field circles against Omicron.

The same is true though more pronounced on the next part of this graph. And here, you see individuals who received as their primary vaccine the AstraZeneca vaccine. Again, in this very large real-world assessment, we can see that mRNA-1273 provides protection against hospitalization due to both Delta but to a lesser extent, Omicron infection.

Of note, we do see waning of protection over time against hospitalization due to Omicron infection, and this fits with the profound immune invasion we know to be the case with Omicron. But it is also a driver of our belief that not only will a booster vaccination be required later in 2022 but also a booster will be required that protects against both the Delta and Omicron variants of concern, as Stephane announced earlier. This is because Delta, as we know, is associated with strong pathogenicity and Omicron, as we have seen, due to its transmissibility and infectivity, is also associated with substantial morbidity and strain on health care systems through sheer bulk of cases, hence protection against both Delta and Omicron may well be necessary in the next booster vaccination.

On Slide 10, we see data directly explaining the clinical phenomenon I just showed you. These data come from one of our previously conducted clinical studies. Sera from individuals immunized and boosted with mRNA-1273 is able to substantially neutralize the ancestral SARS-CoV-2 virus, D614G, shown here in black, but to a lesser extent, Omicron, shown in red. And this is particularly true by 6 months following booster administration. Again, it is these data, coupled with the real-world effectiveness data that I just showed you, that leads us to believe an additional booster dose will be needed later in 2022, providing protection against both Delta and Omicron variants of concern.

You can see this point made clearly again in Slide 11, where we estimate the duration of protection against either the ancestral D614G strain or against Omicron. With lower starting titers, protection against Omicron wanes and forwards to levels that would begin to allow breakthrough infection to occur due to Omicron around 9 months after boosting. As leaders in mRNA vaccines and COVID-19 disease, we will continue to monitor this carefully along with other emerging variants and continue to do whatever we can to provide people with a safe and highly effective vaccine booster for 2022 and years to come. We announced in January that we were able to go from identification of Omicron to testing of a new vaccine in humans in just 2 months. That is a remarkable testament to the Moderna mRNA platform and its utility.

Slide 12 will be familiar to many of you as we first presented this slide at our Vaccines Day in April 2021. The graph is an illustration of the different phases of the pandemic to endemic continuum and its effect as measured by morbidity or disease burden over time. The shape of the graph was adopted from what we knew about previous pandemics at the time and what we expected from the current pandemic, taking into consideration the increased levels of immunity that our immune systems collectively became familiarized with the SARS-CoV-2 virus, either through infection or vaccination. As the graph shows and with hindsight, it is easy to recognize that the very first wave of the pandemic when all of the world's population was naive to this virus caused the highest levels of morbidity and mortality. With each subsequent wave in mid-2021 with Delta and in late 2021 and early 2022 with Omicron, the morbidity observed from these waves tended to be less severe certainly relative to the first wave as our immune systems became more experienced at fighting the SARS-CoV-2 virus.

Beyond 2022, there still remains uncertainty. However, given what we know now of other pandemics like the 1918 influenza pandemic and more importantly, what we have observed with the SARS-COV-2 pandemic, we do believe that we are transitioning into an endemic phase, marked by a period of stability in case counts, hospitalizations and death at least in the Northern Hemisphere. We will continue to carefully monitor the situation in the Southern Hemisphere as winter approaches there on a background of continuing Delta and Omicron infection pressure, and we will work as quickly as possible to generate new specific booster vaccine data.

In the endemic phase, the virus will continue to circulate but at rates that are static and more predictable. We continue to expect morbidity from the virus when it is endemic, and we believe, like other respiratory viruses, we will see a seasonal pattern of disease that emerge. But the good news is, because our immune system is now much more familiar with the virus, either through vaccination, infection or both, we do not expect that the majority of the population will be as susceptible to severe disease in the endemic phase as they were in the pandemic phase. Instead, as with other respiratory viruses, we believe protection from SARS-COV-2 will be critical for populations that are likely to be most susceptible to severe disease and high burden of disease. Providing the broadest protection possible will be a focus for us in the endemic phase, and we believe, as Stephane mentioned, multivalent vaccines against SARS-COV-2 and its variants will help achieve this.

As I alluded to earlier, respiratory viruses cause significant disease annually and endemic coronaviruses are no exception to this. Slide 13 shows the incidence of community-acquired infections leading to hospitalizations in New York City during the 2018 to 2019 season prior to the SARS-CoV-2 pandemic. On the chart, you can see that other endemic human coronaviruses, in fact, cause the highest level of hospitalizations in individuals between 65 and 79 years of age and those 80 years and above, followed by RSV and influenza. Across OECD countries, the estimated impact from endemic human coronaviruses leads to over 1 million outpatient visits, 350,000 hospitalizations and 20,000 deaths in the over 65-year-old population annually.

We believe SARS-CoV-2 will follow a similar pattern of seasonal disease as other respiratory viruses do and will impact vulnerable populations. Protecting populations against SARS-CoV-2 will be critical in the months and years to come. And protecting against combinations of respiratory viruses such as SARS-CoV-2, flu and RSV with a single yearly shot will be central to our strategy. Stephen Hoge will shortly provide an update on our robust ongoing strategy to achieve that.

So in summary, the available real-world data continue to show the remarkable effectiveness of mRNA-1273. Real-world data shows that a 50-microgram booster dose of mRNA-1273 provides protection against hospitalization caused by Omicron, but we note waning of antibody titers by 6 months post boosting. We believe that a fall 2022 booster will be needed globally. And as leaders in mRNA vaccines, we believe it is important to develop booster vaccines that will give us an opportunity to protect against Omicron and future variants as we continue our fight to help end this pandemic.

I will now hand over to Dr. Stephen Hoge to provide further updates on this topic and the Moderna pipeline. Stephen?

Stephen Hoge - *Moderna, Inc. - President*

Thank you, Paul. Good morning and good afternoon, everyone. On Slide 16, I'd like to briefly summarize our COVID-19 booster development strategy for the endemic phase.

As Paul covered, the strategic rationale for a seasonal booster has 3 parts. First, we think neutralizing titers will wane similar to the endemic human coronaviruses, as Paul just described. That decline in neutralizing titers will increase the risk of breakthrough hospitalization in those at higher risk, specifically including older adults and the immune compromised. We think the emergence of new variants of concern will also have the risk of accelerating waning and broadening the risk of breakthroughs to other populations.

So the desired features for our Northern Hemisphere fall and winter 2022 booster are described here. First, we'd like to improve the durability of protection for neutralizing antibodies against Omicron and Omicron mutations to at least 6 months that will provide full protection through the Northern Hemisphere fall/winter infection season. We'd like to retain the high and durable protection we've been seeing with a prototype vaccine against Delta and the ancestral strains. And third, we'd like to broaden cross-protective immunity to the extent possible to increase the potential for protection against a new emergent variant of concern, which could emerge perhaps from the Southern Hemisphere this midyear.

So on Slide 17, I'll quickly summarize our strategy for developing an updated booster for fall 2022. We are currently evaluating 3 different booster strategies in adults aged 18 plus. The first, as both Paul and Stephane have mentioned, is a bivalent booster vaccine made up of the prototype mRNA-1273 and an Omicron-specific mRNA-1273.529. This bivalent has been called 214. We are also evaluating, as we previously announced, an Omicron-specific booster, mRNA-1273.529. And of course, we will continue to evaluate our prototype booster, mRNA-1273, for which there is a large body of real-world evidence, as Paul just described.

We're evaluating these 3 different approaches across 2 studies in the United States and the United Kingdom, a Phase II study in the United States of approximately 750 participants and a 3,000-participant study in the United Kingdom. Both are looking at both bivalent and Omicron-specific boosters, and both will be looking at both third and fourth dose of those boosters. In the U.K. study, we will also be looking at heterologous boosting, including on the background of other mRNA vaccines and non-mRNA vaccines.

Now I'd like to take a moment on Slide 18 to provide some scientific insight to why we believe the bivalent vaccine booster for the fall of 2022 offers a potential advantage. Slide 18 includes data on some of our prior bivalent boosters, and this data -- this emerging data suggest to us that there may be an opportunity to improve durability against variants of concern while preserving activity against the ancestral variants. This data is based on one of our prior bivalents, mRNA1273.211 or 211 for short.

And 211, as you may recall, was based on the 1273 vaccine and the Beta variant of concern, which emerged approximately a year ago. When we compare over time how the 2 different booster strategies, our prototype booster on the left-hand column here, and our bivalent booster on the right-hand column here, do against the 2 different virus variants that were in the vaccine, you see an emergence of potential improvement in durability.

So first, to orient you to the slide. mRNA-1273 was given at 50 micrograms as a booster to those who had previously received 2 doses of mRNA-1273 vaccine. And on the top left panel, you'll see how -- the neutralizing titers or pseudovirus neutralizing titers against the ancestral strain of the virus, D614G virus, in our validated clinical assays. Underneath there, you'll see how those -- the pseudovirus neutralization titers against the Beta variant of concern in blue. And in the middle column, you'll contrast that with the bivalent 211 booster, which, in this case, included the Beta variant of concern, again, at the same dose level, 50 micrograms. Top right panel is the ancestral variant of concern -- the ancestral virus, D614G, and lower right is the Beta variant of concern or the B1.351.

Now as you'll note, comparing the performance against the ancestral D614G virus, both mRNA-1273 and the bivalent Beta-containing booster do a good job boosting neutralizing titers by day 29 after the booster. So 1 month post booster, neutralizing titers are approximately 1,800 for 1273 and 2,200 for the bivalent. And importantly, as we test the serum 6 months after booster, noted as day 181 here, you'll see that neutralizing titers remain high, approximately 1,000 in both boosters.

Now the situation against the variant of concern, in this case, Beta, is slightly different. Again, both boosters increased neutralizing titers by day 29 1 month after booster to quite reasonable levels, approximately 1,000 in both cases. However, when you follow out 6 months, there is a difference in the neutralizing titers that emerges. And not surprisingly, the bivalent booster, which includes the Beta variant of concern, starts to see more durable neutralizing titers, 402, as noted here, as opposed to 154 for mRNA-1273.

So in summary, 6 months after a 211 bivalent booster, the neutralizing titers against the Beta variant of concern appear to be more durable than with just a prototype booster. And the durability or the rate of decline for the Beta neutralizing titers more closely matches that seen for the ancestral virus following the bivalent 211 booster. Including the Beta variant of concern, therefore, appears to be improving the durability of neutralizing titers against that variant of concern.

Now on the next slide, Slide 19, we have that same data but now plotted as a function of time to help you visualize it a little more clearly. On the left-hand side, we're contrasting the mRNA-1273 booster as a black line against a bivalent Beta-containing booster in the red line. On the left-hand side, you're again looking at the ancestral D614G neutralizing titers. And as you can see, following a booster approximately 6 months after dose 2, neutralizing titers for both of the boosters, both bivalent and the prototype vaccine, increased significantly. And the data we have out to 6 months, if you project that forward as we do with the dotted lines, suggest that we will maintain quite high neutralizing titers, perhaps as long as 1 year.

Now the situation on the right-hand side highlights, we think, the potential for improving durability with a bivalent vaccine. Again, here, the black line is mRNA-1273 and the red line is the bivalent Beta-containing booster at the same dose level. Now while both boosters increase neutralizing titers to approximately 1,000 within 1 month of boosting, what starts to emerge 6 months later is a different degree of durability in those neutralizing titers with the bivalent vaccine containing the Beta antigen doing slightly better, as you can see with the red line. And if you project that forward, it suggests that the bivalent vaccine neutralizing titers against the Beta variant of concern will remain quite high, perhaps as long as a year, whereas

with the prototype vaccine, those neutralizing titers appear to be decaying more quickly, back towards baseline levels or pre-booster levels by approximately 8 to 9 months.

On Slide 20, just to quickly summarize therefore where we are on COVID-19 booster development for fall 2022. We believe that a seasonal booster will be necessary to prevent breakthrough diseases, including hospitalization in vulnerable populations. And we believe that the continued evolution of the virus is going to continue to put pressure on pre-existing immunity, whether that's naturally derived or vaccine provided.

We think the fall 2022 booster should reflect the diversity of circulating mutations that are out there in order -- and seek to achieve greater than 6 months of neutralizing titer durability to increase the potential for protection throughout the entire fall season; in this case, we think September through February. So Moderna is developing an Omicron-containing bivalent booster, based on data that we have from prior bivalent candidates that suggests that incorporating the variant of concern and those mutations from that variant of concern, has the potential to improve the durability against such variant of concern.

Now moving to Slide 21, just quickly catching up on other developments in our COVID-19 vaccine. We have made progress in primary series and booster in adolescent and pediatric populations. So in adolescents first.

We've received regulatory approvals for Spikevax in Europe, United Kingdom, Australia, Canada and many other countries. In the U.S., we plan to submit an EUA for 100 micrograms of mRNA-1273 in adolescents that are immune compromised or at elevated risk of severe outcomes. And we're also evaluating the potential of a lower dose, 50 micrograms, as a primary series. And lastly, as has been noted previously, we're preparing to submit data for 50 micrograms as a booster dose in adolescents and 50 micrograms as the booster dose in adults as well, and that will include data on heterologous boosting.

In pediatrics or the 6- to 11-year-old, we've received provisional approval for Spikevax in Australia and submitted to multiple other international regulatory agencies and expect authorization shortly. The U.S. submission is pending alignment with the United States FDA on the adolescent application, and we will also continue to evaluate lower doses, including a 25-microgram primary series dose.

Finally, in the youngest, 6 months to 5 years old pediatric population, we expect data on our 25-microgram 2-dose primary series in the first quarter. And pending that data, we'll plan to submit to regulators. We are also continuing to evaluate lower doses and the potential of a third dose in that population.

Pivoting to the broader respiratory vaccine portfolio on Slide 22. Beyond COVID-19, we continue to make progress across all of our respiratory vaccines. As Stephane mentioned, our flu vaccine is fully enrolled with Phase II. And pending that data, we will prepare to move forward, which we still anticipate doing in 2022, into a Phase III study. We're also preparing to start a combination flu and COVID vaccine, which is currently in preclinical but we expect to start the Phase I study this year.

Our older adult RSV program has started its Phase III study portion, and that pivotal study is ongoing and enrolling. We have a pediatric RSV study which we will move forward in Phase I. We have also 2 different respiratory combination vaccines: first, the human metapneumovirus and parainfluenza virus 3 vaccine, which is in Phase Ib and is now fully enrolled; an RSV plus HMPV vaccine, which remains in preclinical development and we hope to start shortly.

Moving now to latent and public health vaccines on Slide 23. As discussed, CMV continues to enroll in the Phase III CMVictory study. We have also moved forward 2 new latent virus vaccines in the clinical testing. Our EBV vaccine to prevent infectious mononucleosis is in Phase I, and our HIV -- our first HIV vaccine, mRNA-1644, is also in Phase I. We announced 2 new development candidates, which I'll cover briefly in the next couple of slides, against HSV and VZV. And our public health vaccines against Zika and Nipah continue to progress.

Briefly, on Slide 24, I'd like to introduce our -- the first of our 2 new development candidates in the space. mRNA-1608 is our vaccine against herpes simplex virus 2. HSV-2 primarily infects the genitals and establishes lifelong latent infections within the sensory neurons. There's a significant burden of disease in developed markets, including approximately 18 million people who are HSV-positive -- HSV-2 positive in the United States. Globally, that represents about 5% of the population. Primary burden of disease is a reduction in quality of life from recurrent lesions.

Our mRNA-1608 vaccine encodes antigens on the surface of the HSV virus and has been able to induce very strong immune responses, as illustrated in the figure to the right. Neutralizing titers in mice following an HSV-2 vaccine with mRNA-1608 are significantly above the levels seen in human sera from those who are seropositive. This gives us reason to believe that we will be able to provide a significant benefit with this vaccine in this population.

The second development candidate is on the following slide, Slide 25. This is our mRNA-1468 program against herpes zoster or shingles. Herpes zoster is caused by the reactivation of latent varicella-zoster virus or VZV for short. It's principally a disease that's seen as a result of declining immunity in older adults, where protection against VZV decline, leading to reactivation of the virus and painful and very itchy lesions. Herpes zoster occurs in about 1 out of 3 adults in their lifetime, and the incidence is increasing as populations age and particularly increases over the age of 50.

On the right-hand side is previously published data in the Journal of Vaccine on our VZV vaccine; in this case, mRNA-1468. Our vaccine in nonhuman primates was compared against the protein and -- a protein plus adjuvant as a stand-in or proxy for the Shingrix vaccine, which is already approved for this indication. As you note on the right, in nonhuman primates, the mRNA vaccine against gE resulted in significant and elevated neutralizing titers after 2 doses and we believe will provide the basis for a strong potential clinical benefit with mRNA-1468.

Moving now to our therapeutic pipeline. We continue to make progress across a range of different programs. On Slide 26, I'll note a few very quickly. First, our PCV program in Phase I is ongoing and the Phase II is fully enrolled. We expect data in the fourth quarter of 2022. We are also going to provide a bit of an update on the checkpoint vaccine and newly announced development candidate in just a minute.

Highlighting other therapeutic areas. Our VEGF program continues to move forward in Phase II with AstraZeneca. And in rare diseases, our PA and MMA programs continue to enroll in their Phase I, with the Phase I -- first dose-level cohort fully enrolled in PA and continued enrolling of additional cohorts. We also continue to make progress across all of our other preclinical programs in rare diseases, including GSD1a, PKU, CN-1 and the cystic fibrosis program with Vertex.

On Slide 27, I'd like to briefly cover our latest development candidate, a checkpoint vaccine to promote anti-checkpoint T-cell responses in cancer, otherwise known as mRNA-4359. So briefly, the objective of this program is to stimulate effector T cells that target and kill suppressive immune and cancer cells that express high levels of targeted checkpoint antigen. It's been previously identified that there are pre-existing IDO and PD-L1 specific T cells that have been identified in cancer patients, in tumors. IDO and PD-L1 specific T cells can kill and remove the immunosuppressive regulatory Immune cells and cancer cells that overexpress these antigens. It's an important counterbalance that helps liberate the immune response against the tumor.

Our vaccine can expand IDO and PD-L1 specific T cells in preclinical models. And the vaccine-induced direct tumor cell killing can facilitate recognition of tumor-associated antigens by other cytotoxic T cells, leading to more broad tumor kill. Systemic blockade with PD-1 or PD-L1 antibodies may further amplify this effect. We will initially be developing mRNA-4359 against indications including first-line cutaneous melanoma Stage IIIB and first-line non-small cell lung cancer.

With that, I'd like to turn it over to David to walk you through the financials.

David W. Meline - *Moderna, Inc. - CFO & Principal Accounting Officer*

Okay. Thank you, Stephen. We are providing today the analysis of actual 2021 fourth quarter and full year results along with a view of key drivers of financial performance going forward. 2021 was a transformative year for the company as it marked the transition from an R&D-focused entity to a commercial-stage company. I'm very pleased with our performance and wanted to thank all of our employees at Moderna for their dedication and response to the many challenges during this unprecedented company scale-up.

Turning now to Slide 29, starting with an overview of our sales performance. Total product sales in the fourth quarter of 2021 were $6.9 billion, representing 297 million doses delivered to our customers. This compares to sales of $4.8 billion for 208 million doses in Q3 and 199 million doses in Q2. We increased our dose supply in the fourth quarter by 43% compared to Q3 after a relatively stable picture in Q2 and Q3 as we successfully focused on removing bottlenecks in our supply chain network.

Sales of our COVID vaccine have shifted in terms of geographic mix over the course of the year, in line with our expectations and the ramp-up of our international manufacturing capabilities. Sales outside the U.S. to the rest of the world were $6.1 billion in the fourth quarter, reflecting 252 million doses. And sales to the U.S. government were $0.7 billion in the fourth quarter, reflecting 45 million doses sold. For the full year, we sold 807 million doses, resulting in product sales of $17.7 billion. We generated sales of $5.4 billion in the U.S. and $12.3 billion with customers in the rest of the world. Approximately 25% of our delivered doses went to low- and middle-income countries, either through direct sales or facilitated by donations from other customers.

Turning to Slide 30 to go into more detail of our Q4 results. The transformation of Moderna from an R&D-focused biotech company to a commercial-stage business continues to be apparent when reviewing our financial results. The comparison of the fourth quarter of 2021 to prior year is not very meaningful due to the significant growth, which is why I'd primarily focus on the quarter-over-quarter comparison relative to Q3 on this slide.

Total revenue was $7.2 billion in the fourth quarter of 2021 compared to $5 billion in the third quarter and $0.6 billion in the prior year period. The increase of total revenue was driven by the sale of the company's COVID-19 vaccine. Product sales in Q4 2021 were $6.9 billion compared to $4.8 billion in the third quarter, an increase of 44%.

Cost of sales was $952 million or 14% of company's product sales in the fourth quarter compared to $722 million or 15% of product sales in the third quarter. The quarter-over-quarter percentage improvement was driven by favorable manufacturing cost as the average selling price remained relatively stable.

Research and development expenses were $648 million in the fourth quarter compared to $521 million in the third quarter and $759 million in the same period in 2020. The higher spend versus prior quarter was primarily driven by increased clinical trial expenses from our expanding and maturing development portfolio. The decrease in spending compared to 2020 was mainly due to the fact that the prior year number includes approximately $200 million of prelaunch inventory costs.

Selling, general and administrative expenses were $201 million for Q4 compared to $168 million in the prior quarter and $79 million for the same period in the prior year. The growth in spending was driven by the commercialization of our COVID-19 vaccine globally, with continued investments in personnel and outside services in support of the accelerated company build-out.

Provision for income taxes was $542 million in the fourth quarter, following $219 million in the third quarter and an insignificant amount in the prior year. Our effective tax rate for the fourth quarter was 10%. The quarter-over-quarter increase was primarily driven by higher earnings. Let me remind you of the fact that we had a net operating loss carryforward of $2.3 billion at the end of 2020. In 2021, we released the valuation allowance against the related deferred tax assets, which resulted in a nonrecurring full year benefit to our effective tax rate of about 5 percentage points.

We recorded net income of $4.9 billion in Q4 compared to $3.3 billion in Q3, an increase of 46%. This compares to a loss of $0.3 billion in Q4 of last year. Diluted earnings per share for Q4 2021 were $11.29.

Turning now to full year financial results on Slide 31. Total revenue was $18.5 billion for the full year 2021 compared to $0.8 billion in 2020. The significant growth was driven by the sales of 807 million doses of the company's COVID-19 vaccine, resulting in product sales of $17.7 billion. Cost of sales was $2.6 billion or 15% of the company's product sales in 2021, including third-party royalties of $641 million. A portion of the inventory costs associated with this year's product sales was expensed as prelaunch inventory in 2020. If inventories sold for the full year was valued at cost, our cost of sales for the period would have been $2.8 billion or 16% of product sales.

Research and development expenses were $2 billion in 2021 compared to $1.4 billion in 2020. The growth in spending in 2021 was driven by clinical trial expenses for our expanding pipeline and the related organizational build-out. Selling, general and administrative expenses were $0.6 billion for the full year 2021 compared to $0.2 billion in 2020. The growth in spending in 2021 was mainly due to increases in consulting and outside services, personnel-related costs, marketing expense and distributor fees primarily attributable to the company's COVID-19 vaccine commercialization-related activities and increased head count.

Provision for income taxes was $1.1 billion for the full year 2021 compared to an insignificant amount in 2020. The effective tax rate in 2021 was 8%. It was lower than the U.S. statutory rate primarily due to a nonrecurring benefit related to the release of the valuation allowance, the ongoing benefit of the foreign-derived intangible income deduction as well as benefits related to stock-based compensation.

Net income was $12.2 billion for the full year 2021 compared to a net loss of $0.8 billion in 2020. Diluted earnings per share were $28.29 for the full year 2021.

Turning to cash and cash deposits on Slide 32. We ended 2021 with cash and investments of $17.6 billion compared to $15.3 billion at the end of Q3. The increase is driven by our commercial activity. The balance of cash deposits for future product supply was $6 billion at the end of the year compared to $6.7 billion at the end of Q3. The reduction quarter-over-quarter is driven by commercial deliveries against our commitments.

Now turning to Slide 33. Our capital allocation priorities remain unchanged. Our top investment priority has been and will continue to be reinvesting in the base business across multiple areas. For R&D, we have significantly increased our spending in 2021 to approximately $2 billion, and we expect to continue to further increase our spending in this area to advance and accelerate our pipeline, both for existing and new programs. We are also further increasing our investment into our global manufacturing network in digital, automation and AI as well as scaling up our global commercial operations.

Our second investment priority is to seek attractive external investment and collaboration opportunities to further expand the reach of Moderna's technology and capabilities. We are considering attractive opportunities that enable and complement our platform and take a disciplined approach in evaluating potential outside investments. Our announced collaborations with Metagenomi and Carisma Therapeutics fall into this category.

After evaluating internal and external investment opportunities, we then assess additional uses of cash. We announced a $1 billion share buyback program in August of last year, which we completed in January of this year. As part of today's press release, we announced that the Board has authorized a new share buyback program of $3 billion.

Similar to last year, we provide you with a financial framework for 2022, which you will find on Page 34. We have signed advanced purchase agreements for expected delivery in 2022 in the amount of approximately $19 billion and signed option agreements for delivery in 2022 of approximately $3 billion on a probabilitized basis. In 2022, we believe that the SARS-CoV-2 virus will evolve to an endemic phase. And as a result, we expect the timing of sales to be larger in the second half of 2022 than the first half.

Our total cost of sales includes the cost of goods manufactured, third-party royalties as well as logistics and warehousing costs. For the full year 2022, we expect a cost of sales ratio in the low to mid-20s percent range. The increase compared to prior year is driven by an expected increase in manufacturing costs as well as a decrease in expected average selling price per dose. The forecast increase of manufacturing costs is primarily driven by higher costs for fill-finish activities due to an expected shift from pandemic pack sizes to smaller dose and vial presentations. The decrease in average selling price is driven by the forecast increased deliveries to low-income countries.

For R&D and SG&A expenses, we expect full year expenses to be approximately $4 billion, driven by our maturing development portfolio and the global scale-up of the company. Based on current tax laws, we expect our 2022 tax rate to be in the mid-teens as a result of the benefits from foreign-derived intangible income, driven by our international business mix and stock-based compensation deductions. Finally, regarding capital expenditures, we are planning for capital expenditures in the range of $0.6 billion to $0.8 billion as we further build out our manufacturing and general company infrastructure globally.

This concludes my remarks concerning the financial performance. And I now turn the call over to Stephane.

Stephane Bancel - *Moderna, Inc. - CEO & Director*

Thank you, David, Stephen and Paul. Let me now share some thoughts about where we're heading. I am pleased to see how the team is executing on our product strategy.

Priority #1, pan-respiratory annual booster. RSV is already in Phase III. We are waiting for flu data to start the Phase III on flu and start the Phase I on COVID plus flu candidate, mRNA-1073. Priority #2, latent viruses vaccines. With CMV in Phase III, now we have 5 candidates, including VZV against shingles, and more coming. Priority #3 therapeutics. We have a new checkpoint cancer vaccine. And priority #4, expanding our unique mRNA platform to create new medicine.

As I shared in January at the JPMorgan Healthcare Conference, there was a big change in commercial momentum for Moderna between early 2021 and early 2022. In early 2021, both mRNA vaccines looked the same after Phase III data, and now we see strong real-world evidence that Spikevax has long duration of efficacy. In early 2021, we were supply constrained, and now we're getting to a place we continue to scale manufacturing, thanks to investments made last year and are less supply constrained. We have contracts with many governments around the world, but in early 2021, we have a few team members on the ground in most countries.

On Slide 37, you can see that Spikevax booster market share has increased across key markets. You see that shift in market share data from around the world where we have teams on the ground. Even in Germany, where there is national mRNA champion, we have moved our share of the booster market from 4% in October 2021 to almost 40% in January 2022. And it is also clear that OECD countries or high-income countries have become de facto mRNA market.

We have continued to increase our signed APAs to now around $19 billion. We also have approximately $3 billion in probabilized options. We continue to have numerous discussions with government and NGOs around the world. For example, the current U.S. contract has its last shipments coming before the summer of 2022. This means that in the $19 billion plus $3 billion option, there is currently no APAs for the U.S. for the second half of 2022. As David mentioned, when we shift into endemic, we expect seasonality in sales. This year, we expect to see continued primary vaccination and boosting in the Southern Hemisphere in the first half and a shift to boosters as a fourth dose booster in the Northern Hemisphere in the second half of the year, similar to flu vaccines.

We were pleased to announce last week a big expansion of our commercial network. From our current 11 countries where we have Moderna commercial teams on the ground, we announced an additional 10 countries: in Europe, Poland, Netherlands, Belgium, Sweden, Norway and Denmark; and in Asia, Malaysia, Taiwan, Singapore, Hong Kong.

You have seen the impact of our strong real-world evidence data, coupled with teams on the ground, drive greater Moderna market penetration. I believe the same phenomena will happen in those 10 new markets.

With a direct commercial presence in these 21 important markets, we'll maximize the impact of Spikevax and also have the teams to launch our pan-respiratory annual booster or latent virus vaccines and the rest of the portfolio. That commercial coverage and capabilities will prove critical in our ability to maximize our impact on patients and the resulting value creation. We now have distributors in Central and Eastern Europe. We have distributors in Asia Pacific and with this week announcement, in Latin America. We, of course, continue to work with COVAX to provide access to our vaccines to low-income countries.

Strategically, we want to create a new business model with governments around -- for pan-respiratory annual booster. We have started to create a subscription or service model with governments around the world. We have announced memoranda of understanding with the governments of Canada and Australia. We are currently in discussions with several other countries. These are 10-year agreements for the supply of pan-respiratory annual booster. We have also governments which have signed APAs for 2023, as you can see on the slide. Numerous discussions are ongoing as we speak about securing supply for 2023 for the endemic setting to protect people at risk: 15 years old and above, people with comorbidity factors, people whose job put them at risk and adults who simply do not want to get severe disease.

As we shared in the past, this is our strategy for capital allocation. As David said, the priority #1 is and remains to invest in the company. We have this unique mRNA platform, and we have $17 billion to invest to grow our pipeline to launch new medicine and to expand the capabilities of our platform. Priority #2 is to expand the platform by in-licensing or M&A as we see new interesting nucleic acid technologies that can complement and strengthen the Moderna platform. Priority #3 is to return capital to shareholders. After completing our August 2021 $1 billion share buyback plan and reducing our share count for the first time, we announced this morning a new $3 billion share buyback.

As we grow Moderna, we care deeply about building the right company which is a responsible company to its community. In 2021, 25% of doses we shipped were to low- and middle-income countries. We're investing in Moderna Science Center in Cambridge and launching an AI academy.

We plan to achieve net 0 carbon emissions globally by 2030. We've announced Moderna Charitable Foundation and the global fellowship program. And we announced plans to invest up to $500 million in manufacturing facility in Africa. We hope to be able to announce some positive developments soon about these exciting projects. We will continue to [put importance on] corporate social responsibilities and share this with you.

Before taking your questions, we'd like to remind you of 2022 events. March 24 will be our Annual Vaccine Day. May 17 will be our Annual Science Day, where we'll present new platform advances. September 8 will be our Annual R&D Day, where we present development pipeline key updates. And today, we're announcing that we'll be hosting our first ESG Day on November 10.

I would like to close by sharing how excited we are about the future of our company. Because mRNA is an information molecule, we always knew this will be a company with 0 drug approach or not. Well, now we know which future it will be.

We are passionate about our ability to have a profound impact on humanity. We believe nobody should be hospitalized because of a respiratory virus. We have the technology to do that. We believe nobody should have medical consequences short term or long term because of a latent virus. We have a technology to do that. We believe we can have a profound impact on disease treatments with our therapeutics first and then our gene-editing programs. This is just the beginning.

Operator, we'll be happy to take your questions.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Our first question comes from Salveen Richter with Goldman Sachs.

Salveen Jaswal Richter - *Goldman Sachs Group, Inc., Research Division - VP*

Outside of the flu data that we're going to see this year, we're going to get personalized cancer vaccine data as well as rare disease data. Could you just speak to, in rare disease, what success would look like and what the regulatory path there could be; and then for the personalized cancer vaccine, whether we would be able to get a sense of proof of concept this year?

Stephen Hoge - *Moderna, Inc. - President*

Sure. Thank you for the question, Salveen. So first, in the rare disease space, it's important to recognize that these are Phase I/II studies, both the PA and MMA study. And I'll speak to the PA study mostly because, as I said a moment ago, it's the one that is -- has enrolled its first cohort and is moving forward with enrollment.

So first and foremost, we are going to be looking at safety in these studies, as you'd expect from a Phase I/II. And so one of the most important things to establish is can we continue to dose, unfortunately, very ill people and ill children in the case of both of these studies with mRNA LNPs for up to 6 months or even longer if they stay on the open-label extension. And establishing the safety of the platform on chronic dosing repeatedly over 6 to 12 months is an important objective of that part of the study.

When it comes to efficacy, again, these are early studies and small in number as usually is the case with rare diseases. And so I have to be careful about interpreting any of the data from the early clinical reads too concretely. But the things we'll be looking for, first and foremost, we'll be looking at the performance of the medicines in terms of preventing clinical outcomes. And so in the case of propionic acidemia, these will be major metabolic

decompensation events or hospitalizations that do happen with some regularity, unfortunately, for those folks who suffer from these rare diseases or diseases like PA.

And we will also be looking at biomarkers and so specifically, biomarkers that have correlated with preclinical disease and perhaps to a lesser extent, with some of the existing transplant-based therapeutic interventions in these diseases. But it's important to note that across all of these things in the biomarker space, there are not, unfortunately, validated biomarkers for these diseases because there have not yet been therapeutics approved. And so it will be a balance between looking at efficacy signals early, to be fair, potential signals of improvements in clinical outcomes and looking at biomarkers across a relatively small number of individuals. And so there will be heterogeneous disease, both genetically and in terms of their performance.

Our hope is when we get composite of data that's clear, that we'll be able to then present that and have discussions with regulators, which is the second part of your question, and have a discussion about what outcomes matter most for a potential pivotal study if we continue forward. But we do believe that the things that will ultimately matter most are clinical outcomes and so the prevention of major decompensation events and hospitalizations and obviously, although the studies will be small in patient number, perhaps even hospitalization and death. So we'll be looking for those sorts of signals from our early studies.

But it's important to recognize, as I said a moment ago, these are relatively small in number and we'll want to be circumspect in how we move forward into those efficacy studies. And those regulatory consultations will be based on those data, and we'll provide updates when we have it.

On the PCV program, as you said, we have completed enrollment in the Phase II study of PCV. And we expect that, that PCV -- as a reminder, that is a head-to-head comparison of KEYTRUDA alone versus KEYTRUDA plus vaccine. And we're looking at relapse-free survival in approximately 1 year. That data we would expect to come in the fourth quarter of this year.

And because it is a randomized head-to-head study, I could provide a clear signal of the potential benefit of personalized cancer vaccines versus KEYTRUDA alone, which is obviously the standard we're going for. That data would emerge based on when we complete enrollment and announce that completement in the fourth quarter of this year. And based on that data, we would consult with regulators and obviously decide how to proceed forward if it's positive.

Operator

Our next question comes from Gena Wang with Barclays.

Huidong Wang - *Barclays Bank PLC, Research Division - Research Analyst*

I have 2 questions. So the first one is regarding the flu data, the Phase II data in early 2022. Can you be a little bit more specific on timing? And what kind of data you think that could be fileable without the need of a Phase III trial with the efficacy outcome?

The second question is regarding the 1273 U.S. aged 12 to 17. In the press release, you said FDA has not concluded on benefit/risk profile of 100-microgram primary series. What additional data you would need to provide? And will you need to provide 50-microgram data in order to receive approval?

Stephen Hoge - *Moderna, Inc. - President*

Great. Thank you, Gena, for both those questions. So first, a clarification on the flu data. We do not believe that the Phase II data alone would be fileable. And that's based on previously published regulatory guidance, not specific guidance to Moderna, that ultimately, we don't think Phase II on flu alone, which is an immunogenicity -- safety and immunogenicity study of approximately several hundred, is sufficient for filing.

The question is, from a filing perspective, what sorts of Phase III studies are necessary and whether or not an accelerated approval is possible based on just safety and immunogenicity or whether we will need to demonstrate efficacy in an independent efficacy study, a Phase III efficacy study prior to filing. And those are consultations that have not yet happened with regulators but will on the back of that Phase II data that we expect shortly. It's important to note that there are precedents for accelerated approvals based just on safety and immunogenicity in a Phase III study, which would be a few thousand people. But you always have to then follow up with an efficacy study perhaps post approval.

And so in summary, we expect to have to do an efficacy study in flu at some point. The question is whether or not it would be before or after accelerated approval with a Phase III immunogenicity and safety study. That Phase III study would follow on the current Phase II study, and we don't think that the Phase II study alone is fileable. We do intend, as I said previously and we've said before, to try and start those Phase III studies, whether they're efficacy, safety, immunogenicity study, this year.

On the question of the 1273 adolescent filing within the U.S., and so the FDA has not provided -- has not completed its review of the 100-microgram adolescent primary series. And we have decided on consultation with them to evaluate a lower dose, a 50-microgram primary series dose in -- of adolescents 12 to 17. It's important to note that the 12 to 17 adolescent 100-microgram primary series has been approved globally in many other markets and we believe has been administered quite broadly, perhaps up to over 1 million adolescents globally. And so we'll continue to collect that real-world data as well as the observational data from our monitoring studies and as and when appropriate, submit that to the FDA for their continued evaluation of the 100-microgram primary series.

We are in the interim -- given the strong real-world efficacy data that we've seen for Spikevax or mRNA-1273 particularly in immune-compromised population, we are in the interim preparing an EUA filing in the United States for 100 micrograms for immune-compromised adolescents or those at high risk of severe outcomes from disease because we think the strong efficacy profile of mRNA-1273 at 100 micrograms provides a clear benefit/risk in that population. We do believe that 100 micrograms provides a benefit more broadly, which is why it's been authorized globally, but we'll continue to work with the FDA and the U.S. to evaluate other potential dose-sparing strategies and submit that data as we develop it.

Operator

Our next question comes from Matthew Harrison with Morgan Stanley.

Matthew Kelsey Harrison - *Morgan Stanley, Research Division - Executive Director*

I have 2 clarifications and then a question. So first one, on flu. Should we expect that when you present to us the Phase II data, whether or not you'll have had those regulatory discussions, we'd be able to talk about potential next steps in terms of what scope of Phase III studies you would need? And then second, on PA, can you give us a sense of how many cohorts you think you need to see before you may be able to provide that initial data?

And then third, just on the timing of COVID revenues this year. I believe at JPM, you had talked more about first half weighting than second half weighting, and it seems like that's switched. And I've gotten just a couple of questions that I thought would be helpful to clarify. Is that mainly because you're now targeting boosters for the fall? Or is there something else happening here in terms of the weighting of the revenues?

Stephen Hoge - *Moderna, Inc. - President*

So thanks, Matthew. I'll take the first 2 questions. So first, on flu, it's obviously not in our hands alone, we will -- whether we would be able to connect with the FDA and get feedback back. As we all know, the agency globally but also the agency in the United States, agencies are -- have a lot going on right now. And so there may be some delays in getting that feedback.

So it is not -- we will probably share the Phase II data as we have it. And we will obviously rapidly consult with agencies, but we will not gate on hearing back from agencies before we share that data. And our plans are moving forward. But if it's possible to get that response more quickly,

obviously, that will be something we'll share at that time. So I wouldn't expect it is the short version, being able to have that agency feedback. But it's possible, and we'll keep our fingers crossed that perhaps the agencies can turn that around more quickly.

On PA, so the number of dose-level cohorts. I think it's important to say that there are sort of 2 features here that we'll be looking at: obviously, the dose-level cohorts, so how many different dose-level or dose-frequency cohorts that we're looking at in that study; but also then, the duration of time on that study because the primary objective of the intervention -- of the PA program particularly is to prevent the major metabolic decompensations. And so that is also something that requires time to accrue so that you can understand, within an individual patient, whether you've changed the rate of those recurring events.

And so it's a mix of 2 things. I mean, I think we would probably expect to see 2 to 3 dose-level cohorts. But also, given the rate of enrollment, that would probably also allow us to accrue approximately 1 year on drug for many of the early recipients. And that combination, those who've been on for a while as well as seeing what dose escalation can achieve perhaps in biomarkers, will be the composite data that we think will allow us to make a determination whether we've got the right dose level and whether we've got a clear indication of benefit and obviously, whether or not we're seeing chronic safety and tolerability, which we will expect. And if we have that data and it feels clear, then we will move to regulatory consultation on the next step of clinical studies and obviously, update all of you with that information. So not a concrete number of dose-level cohorts but more a function of both time on drug for the early cohorts and perhaps a second or third dose-level cohort of data that will provide us with that clarity.

And I'll turn it over to, I think, David for the third question.

David W. Meline - *Moderna, Inc. - CFO & Principal Accounting Officer*

Yes. So in terms of the first half, second half timing, as we've looked now at -- as we move into '22, what do we see? We see that the emerging market countries of COVAX have indicated that they're having a lot of challenge to absorb all the product that they're receiving through donations. And therefore, as we looked at in particular the second quarter timing versus the third quarter, we refined that outlook to be, as I described, first half, second half. And then secondly, the second half is certainly -- as Stephane mentioned, we think there's going to be quite strong booster sales that will cause the second half to be a bit higher than the first half.

Operator

Your next question comes from Michael Yee with Jefferies.

Michael Jonathan Yee - *Jefferies LLC, Research Division - Equity Analyst*

We had a 2-part question. One was thinking about your COVID booster strategy and the 3 different strategies you laid out, including the bivalent, which I think is great. Can you just talk about at what point you would decide to pick which strategy that would be and you're confident that whatever that would be, that, that would be ready and able to be approved by the FDA to distribute presumably for the fall 2022 booster season and if that is actually the product that would be in the guidance for 2022?

And the second question relates to U.S.A. I know previously you had talked about U.S.A. boosting options and purchases. But I can't actually remember what or where we are for U.S.A. for 2022 or for 2023. And maybe just speak to the color about that market.

Stephen Hoge - *Moderna, Inc. - President*

Great, Michael. So I'll take the first question and perhaps turn it over to Stephane for the second. So in terms of the strategy, so the most important thing to start with maybe is that 1273 as a booster already exists. And so that is a booster candidate. Although we're evaluating it as a fourth dose, we'd expect to have that safety data relatively quickly and immunogenicity data, and we've seen strong real-world evidence of mRNA-1273. And

so that booster candidate is obviously something that's well known to markets and could be available quite quickly. We're evaluating the Omicron-specific and the Omicron-containing bivalent or 214 in 2 studies that are ongoing right now.

Now the challenge with all of that, and I think it's where your question is going, is that when you're trying to evaluate durability -- a difference in durability, that takes time. And so while we're running these studies, both the Omicron and Omicron-containing bivalent, and we expect to have data in the first half of this year that would be 1 month post boost and we could turn around and establish, we believe, the safety and the potential benefit of those boosters and we would hope that the bivalent would continue to be even more compelling, the challenge is that it's going to be very hard to achieve 6 months of durability data before Q3. And that's just a function of time. If you boost people now, it will take time to get that day 181 or 6-month durability data that we've already started to show with our bivalent vaccines.

And so the question then becomes how do we proceed from a filing perspective if we're aiming at the fall for 2022. And those are consultations that are ongoing with regulators now. We do have the benefit of having tested multiple previous bivalent vaccines, and we do have the benefit of being able to use the 6-month follow-up data there to start to evaluate this potential for better durability. And so you could imagine a world where we proceed with the 1-month data on our bivalent vaccine showing safety and non-inferiority perhaps against the existing variants, including perhaps the circulating variant of concern known as Omicron, and that we follow up over time, perhaps in the early part of the fall, with data that would confirm the improvement in durability. And then we would rely on the fact that the previous bivalent vaccines like mRNA-211 had shown that benefit of durability against previous variants of concern, including some that contain some of the same mutations seen in Omicron.

And so it's a relatively complicated picture because we all -- we do believe, as we've said, that it is time to update the vaccine against the mutations that are currently circulating and to improve the durability against those new variants of concern, but it does run into the challenge of timing of those filings. And so those consultations with regulators are ongoing, and we'll provide updates as we align with them on the path forward. That's quite different than the public health decision from governments as to which vaccines they may want to prepare to stockpile in advance of a fall booster season, which likely can proceed in parallel even without the regulatory filings as it has in the past as it did during the original first wave of the pandemic.

So with that, maybe I'll turn it over to Stephane to talk about the fall in the U.S.

Stephane Bancel - *Moderna, Inc. - CEO & Director*

Thank you, Stephen. So let me maybe talk about it in 2 angles. The first one is, as we've said this morning, in this increased APAs we've announced at $19 billion, there is no signed APA for -- between Moderna and the U.S. government. So the number in there from the U.S. is 0. And because there's no option either that the government has from a previous contract, the U.S. government has no option currently. So there is $0 in the $3 billion of options probabilized.

What is not clear today is what would the U.S. government decide to do for the fall of 2022. Will they, like they have done in '20 and '21, buy vaccines from the manufacturers and give them away for free, I believe, for first, second and third dose? Will it be a private market? Or will it be a mix of both private and free vaccine available? Because you could see where we are, if we can sell to private markets, private networks and even companies that might want to procure the vaccines and that's the bit that is not clear. So it is why, in a very conservative manner, because what we have communicated so far are signed APAs or options and because the U.S. government has 0, we did not include any of those numbers.

Operator

Our next question comes from Cory Kasimov of JPMorgan.

Cory William Kasimov - *JPMorgan Chase & Co, Research Division - Senior Biotechnology Analyst*

First one, I just want to follow up on what you were just discussing and just kind of looking beyond this fall though and as kind of we think about moving into this endemic phase and how you're thinking it's evolving. Regarding the outlook for the commercial marketplace and like 2023 plus,

do you expect APAs for larger countries, be it the U.S. or Europe or anywhere else? Or do you think you'll be doing more selling into private markets? In other words, is there any reason not to shift away from an APA structure?

And then secondly, just on capital allocation. Recognize your priorities remain the same here, and clearly, with 44 programs in development, new subsidiaries opening around the world, you have enough capital to do many things simultaneously. But how should we think about priorities with nearly 20% of your year-end cash being dedicated to this latest buyback? Is that 15% to 20% range of kind of your balance sheet an appropriate number to be thinking about in the future?

Stephane Bancel - *Moderna, Inc. - CEO & Director*

So let me take the first question, Cory, and I'll turn to David for the buyback question. So if you look at the countries outside the U.S., they are in, let's say, non-dynamic markets. They are mostly direct contract with governments anywhere. So what it is going to look like in terms of shape and form is not very clear. For example, Europe has purchased together the vaccines for the pandemic, which is not the case, let's say, for seasonal flu, for example. So will they continue that model for COVID and move to that model for other vaccines or would they go back to a national system is to be seen. But all countries like Japan, Canada and so on are basically a single-buyer market. Some countries, there's small private markets but it's mostly kind of government orders.

And so we are in discussions with governments about '23. As you saw, we've already signed contracts for '23 because some countries like the U.K. and others wanted to secure supply because they believe very deeply that the endemic market will require annual boosters. And so we just want to get ahead of it.

And as you saw with what we are doing with Canada and Australia, which I think is a very interesting new model of kind of service-based, subscription-like partnership, is we basically are trying to secure, as we said, 10-year agreements. And we're in discussion with several more countries about setting the similar model in the countries where we build a plant. They will reserve a given volume for a year, let's say, $20 million, $50 million, $100 million, depending on the market size. And then what we commit to them is to be able to customize the respiratory vaccines with what they believe they want.

So as you saw from Paul's presentation, there's a lot of respiratory virus that most people are not aware of even their names. Look at PIV. Very few people knew that there were coronaviruses circulating and creating so much hospitalization and deaths every year. Well, our vision is to bring all of those components together and discuss with local public health experts, on an annual basis, what do they want in their vaccine for Canada or vaccine for Australia.

As we discussed on the flu call in the fall, sometimes, WHO picks a flu strain like H3, or -- and then it's a different flu strain that winter that is between, let's say, North America, Europe and/or Asia, like Japan and so on. And so this ability to also customize and -- work with local public health authorities to customize a vaccine they want, we think it's a really unique feature of this platform because of the speed, because of ability to combine components.

And so that's what we're already trying to do here, is to really establish very long-term agreements. I am not aware of other companies having done this type of agreement in pharma. And I think this is something we can do and that the teams are working very actively also. We'll have to wait a few more months to see more coming, but there are quite a lot of discussion. We just have to wait for that because we cannot do 10 countries at the same time in discussion because they are very customized and very complex partnerships. But that's exactly where we're trying to go ahead.

David, do you want to talk about our thinking about buybacks?

David W. Meline - *Moderna, Inc. - CFO & Principal Accounting Officer*

Sure, yes. Yes. I mean, I guess what I'd say about the announcement today, I think what you need to think about is a few things as we did. So why $3 billion? Why now? It starts with a few things. One is, as we said, investing internally and externally and ensuring that we have plenty of firepower

to allow us to do that. So clearly, where we enter 2022, we're in a good position to fund all of the opportunities that we think we have and they're very compelling. So that's one.

Two is looking at what visibility we have of additional cash generation for the company. And again, we feel very good about that certainly as we enter 2022. And then thirdly, we look at the valuation levels, and certainly, we think this is quite attractive at these levels. So combination of all that adds up to an announcement of $3 billion.

To your question, should I be filling in the model for that to continue on an ongoing basis? I think it's a little bit early for us to comment right now on that question. And I'd encourage you just to wait and let's see how this evolves. But we feel very good about the prospects for the business. I think the statement today is one of a strong confidence that we can achieve all of the objectives that we've set out for the company.

Operator

Our last question comes from Tyler Van Buren with Cowen.

Tyler Martin Van Buren - *Cowen and Company, LLC, Research Division - Analyst*

On a similar topic of conversation, can you just provide your latest thoughts on future U.S. pricing for Spikevax? Do you expect future contracts to have pricing that has normalized relative to ex-U.S. countries?

And maybe just on a second point to clarify. Do you believe that a new variant wave emerging by year-end is necessary to record the vast majority of the $3 billion in APA options?

Stephane Bancel - *Moderna, Inc. - CEO & Director*

So let me start. So I will not comment on the U.S. pricing for obvious reasons, because of our discussions with the government. I think as we said before, once this goes into normal private market, we do expect the pricing to be higher. We think the vaccine does not reflect -- sorry, the price doesn't reflect the value of a vaccine from a pharmacoeconomic standpoint.

And I mean the options, the $3 billion, so they are just different stage. Some are just waiting funding from governments to move into fully signed APAs. Some are things with COVAX that has placed orders for future needs. So I don't think there needs to be a new variant for some of it to happen and plus the U.S. on top of that.

But again, we have never managed through a pandemic and through a transition from pandemic to endemic. So otherwise, we want to be cautious and prudent. But I think it doesn't need a new variant for a material chunk of the $3 billion to move into signed APAs.

Operator

Ladies and gentlemen, this concludes the Q&A portion of today's conference. I'd like to turn the call back to Stephane for any closing remarks.

Stephane Bancel - *Moderna, Inc. - CEO & Director*

Well, thank you very much everybody for joining. I look forward to talking to you in the coming days and weeks and especially to welcome you at our Vaccine Day, which will be exciting, in March. Thank you.

Operator

Ladies and gentlemen, this does conclude today's presentation. You may now disconnect, and have a wonderful day.